Clinical trial results:
A Randomized, Active-Controlled, Dose-Ranging Estimation Study to Evaluate the Safety, Tolerability, and Efficacy of Different Regimens of MK-5172 When Administered Concomitantly with Peginterferon alfa-2b and Ribavirin in Treatment-Naïve Patients with Chronic Genotype 1 Hepatitis C Virus Infection

Summary

EudraCT number	2011-000759-18
Trial protocol	DE BE IT
Global end of trial date	10 March 2015

Results information

Result version number	v1 (current)
This version publication date	26 February 2016
First version publication date	26 February 2016

Trial information

Trial identification

Sponsor protocol code	5172-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01353911
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration: MK-5172-003

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the safety, tolerability, and antiviral activity of grazoprevir (MK-5172) when administered in combination with peginterferon (Peg-IFN) and ribavirin (RBV) in treatment-naïve (TN) participants with chronic hepatitis C.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	United States: 255
Worldwide total number of subjects	368
EEA total number of subjects	57

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	353
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

368 participants enrolled on study. 36 cirrhotic participants received open-label (OL) grazoprevir + peginterferon (Peg-IFN) + ribavirin (RBV), and 332 non-cirrhotic participants were randomized to receive 100, 200, 400, or 800 mg grazoprevir + Peg-IFN + RBV. 43 in the 400 mg group and 36 in the 800 mg group were down-dosed to 100 mg grazoprevir.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	OL Grazoprevir 100 mg

Arm description:

Treatment-naïve (TN) cirrhotic participants received open-label Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Arm type	Experimental
Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300 mg to 700 mg orally twice daily.

Arm title	Grazoprevir 100 mg

Arm description:

TN non-cirrhotic (NC) participants received Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Arm type	Experimental

Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300 mg to 700 mg orally twice daily.

Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules orally three times daily.

Arm title	Grazoprevir 200 mg

Arm description:

TN NC participants received Grazoprevir 200 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Arm type	Experimental
Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details: 300 mg to 700 mg orally twice daily.	
Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Four capsules orally three times daily.	
Arm title	Grazoprevir 400 mg
Arm description: TN NC participants received Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Arm type	Experimental
Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Orally once daily in AM. Blinded or open-label depending on treatment arm.	
Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: 1.5 µg/kg/week subcutaneous injection.	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 300 mg to 700 mg orally twice daily.	
Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Four capsules orally three times daily.	
Arm title	Grazoprevir 800 mg
Arm description: TN NC participants received Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Arm type	Experimental

Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300 mg to 700 mg orally twice daily.

Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules orally three times daily.

Arm title	Grazoprevir 400 mg/100 mg

Arm description:

TN NC participants initially were randomized to receive Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Arm type	Experimental
Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300 mg to 700 mg orally twice daily.

Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules orally three times daily.

Arm title	Grazoprevir 800 mg/100 mg

Arm description:

TN NC participants initially were randomized to receive Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Arm type	Experimental
Investigational medicinal product name	Grazoprevir
Investigational medicinal product code	
Other name	MK-5172
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally once daily in AM. Blinded or open-label depending on treatment arm.

Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 µg/kg/week subcutaneous injection.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300 mg to 700 mg orally twice daily.

Investigational medicinal product name	Placebo for Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules orally three times daily.

Arm title	Boceprevir 800 mg

Arm description:	
TN NC participants started a 4 week lead-in with Peg-IFN + RBV, then received Boceprevir 800 mg + Peg-IFN + RBV for 24 weeks followed by 0 or 20 weeks of Peg-IFN + RBV, based on response guided therapy.	
Arm type	Active comparator
Investigational medicinal product name	Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Four 200 mg capsules orally three times daily.	
Investigational medicinal product name	Peg-interferon alfa-2b
Investigational medicinal product code	
Other name	PegIntron™
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1.5 µg/kg/week subcutaneous injection.	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Rebetol™
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
300 mg to 700 mg orally twice daily.	
Investigational medicinal product name	Placebo for Grazoprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Orally once daily in AM.	

Number of subjects in period 1	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg
Started	36	66	68
Completed	28	57	59
Not completed	8	9	9
Status Not Recorded	4	-	1
Consent withdrawn by subject	2	3	4
Lost to follow-up	2	6	4

Number of subjects in period 1	Grazoprevir 400 mg	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg
Started	24	29	43
Completed	22	23	36
Not completed	2	6	7
Status Not Recorded	-	-	-

Consent withdrawn by subject	2	2	3
Lost to follow-up	-	4	4

Number of subjects in period 1	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Started	36	66
Completed	30	51
Not completed	6	15
Status Not Recorded	-	-
Consent withdrawn by subject	3	9
Lost to follow-up	3	6

Baseline characteristics

Reporting groups	
Reporting group title	OL Grazoprevir 100 mg
Reporting group description:	
Treatment-naïve (TN) cirrhotic participants received open-label Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 100 mg
Reporting group description:	
TN non-cirrhotic (NC) participants received Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 200 mg
Reporting group description:	
TN NC participants received Grazoprevir 200 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 400 mg
Reporting group description:	
TN NC participants received Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 800 mg
Reporting group description:	
TN NC participants received Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 400 mg/100 mg
Reporting group description:	
TN NC participants initially were randomized to receive Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 800 mg/100 mg
Reporting group description:	
TN NC participants initially were randomized to receive Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Boceprevir 800 mg
Reporting group description:	
TN NC participants started a 4 week lead-in with Peg-IFN + RBV, then received Boceprevir 800 mg + Peg-IFN + RBV for 24 weeks followed by 0 or 20 weeks of Peg-IFN + RBV, based on response guided therapy.	

Reporting group values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg
Number of subjects	36	66	68
Age categorical Units: Subjects			

Age Continuous | Units: years			
arithmetic mean	54.4	46.4	48.3
standard deviation	± 6.9	± 11.3	± 10.6

Gender, Male/Female Units: participants			
Female	14	25	32
Male	22	41	36

Reporting group values	Grazoprevir 400 mg	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg
Number of subjects	24	29	43
Age categorical Units: Subjects			

Age Continuous | Units: years			
arithmetic mean	44.6	50.4	48.3
standard deviation	± 12.5	± 13.4	± 11.4
Gender, Male/Female Units: participants			
Female	12	15	15
Male	12	14	28

Reporting group values	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg	Total
Number of subjects	36	66	368
Age categorical Units: Subjects			

Age Continuous | Units: years			
arithmetic mean	50.3	48.3	
standard deviation	± 11.2	± 11.2	-
Gender, Male/Female Units: participants			
Female	13	29	155
Male	23	37	213

End points

End points reporting groups

Reporting group title	OL Grazoprevir 100 mg
Reporting group description:	
Treatment-naïve (TN) cirrhotic participants received open-label Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 100 mg
Reporting group description:	
TN non-cirrhotic (NC) participants received Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 200 mg
Reporting group description:	
TN NC participants received Grazoprevir 200 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 400 mg
Reporting group description:	
TN NC participants received Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 800 mg
Reporting group description:	
TN NC participants received Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 400 mg/100 mg
Reporting group description:	
TN NC participants initially were randomized to receive Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Grazoprevir 800 mg/100 mg
Reporting group description:	
TN NC participants initially were randomized to receive Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.	
Reporting group title	Boceprevir 800 mg
Reporting group description:	
TN NC participants started a 4 week lead-in with Peg-IFN + RBV, then received Boceprevir 800 mg + Peg-IFN + RBV for 24 weeks followed by 0 or 20 weeks of Peg-IFN + RBV, based on response guided therapy.	

Primary: Percentage of Participants Achieving Complete Early Viral Response (cEVR)

End point title	Percentage of Participants Achieving Complete Early Viral Response (cEVR)[1]
End point description:	
Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. The Roche COBAS Taqman HCV Test, v2.0 assay (High Pure System) had a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL (in plasma). cEVR was defined as undetectable HCV RNA (target not detected [TND]) at Week 12. 95% confidence intervals provided based on the Clopper-Pearson method. A Missing = Failure approach was used for missing data. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg	

regimens.

End point type	Primary

End point timeframe:

After 12 weeks of treatment with grazoprevir/boceprevir

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no formal efficacy hypothesis testing planned for this endpoint, and there were no between-group statistical comparisons performed.

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[2]	66[3]	68[4]	24[5]
Units: percentage of participants				
number (confidence interval 95%)	94.4 (81.3 to 99.9)	80.3 (68.7 to 89.1)	85.3 (74.6 to 92.7)	87.5 (67.6 to 97.3)

Notes:

[2] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[3] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[4] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[5] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[6]	43[7]	36[8]	66[9]
Units: percentage of participants				
number (confidence interval 95%)	75.9 (56.5 to 89.7)	86 (72.1 to 94.7)	86.1 (70.5 to 95.3)	69.7 (57.1 to 80.4)

Notes:

[6] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[7] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[8] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

[9] - Full Analysis Set (FAS); all randomized/enrolled participants receiving ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Adverse Events (AEs) During the Treatment Period and First 14 Follow-up Days

End point title	Percentage of Participants Experiencing Adverse Events (AEs) During the Treatment Period and First 14 Follow-up Days

End point description:

An AE was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the SPONSOR’s product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the SPONSOR’s product, was also an AE. Participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Primary

End point timeframe:

Treatment period plus the first 14 days of follow-up (up to 50 weeks)

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[10]	66[11]	68[12]	24[13]
Units: percentage of participants				
number (not applicable)	94.4	98.5	97.1	95.8

Notes:

[10] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[11] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[12] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[13] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[14]	43[15]	36[16]	66[17]
Units: percentage of participants				
number (not applicable)	96.6	97.7	97.2	97

Notes:

[14] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[15] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[16] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

[17] - All Participants as Treated (APaT); all randomized/enrolled receiving ≥1 dose of study treatment.

Statistical analyses

Statistical analysis title	Grazoprevir 100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 100 mg v Boceprevir 800 mg
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	9.1

Statistical analysis title	Grazoprevir 200 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in

combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 200 mg v Boceprevir 800 mg
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	7.9

Statistical analysis title	Grazoprevir 400 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 400 mg v Boceprevir 800 mg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.6
upper limit	7.2

Statistical analysis title	Grazoprevir 800 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 800 mg v Boceprevir 800 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	7.7

Statistical analysis title	Grazoprevir 400 mg/100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 400 mg/100 mg v Boceprevir 800 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	8.5

Statistical analysis title	Grazoprevir 800 mg/100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants with at least one AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 800 mg/100 mg v Boceprevir 800 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	8.1

Primary: Percentage of Participants Who Discontinued Study Medication Due to AEs During the Treatment Period and First 14 Follow-up Days

End point title	Percentage of Participants Who Discontinued Study Medication Due to AEs During the Treatment Period and First 14 Follow-up

	Days

End point description:

An AE was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the SPONSOR's product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the SPONSOR's product, was also an AE. Participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Primary

End point timeframe:

Treatment period plus the first 14 days of follow-up (up to 50 weeks)

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[18]	66[19]	68[20]	24[21]
Units: percentage of participants				
number (not applicable)	5.6	4.5	5.9	8.3

Notes:

[18] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[19] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[20] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[21] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[22]	43[23]	36[24]	66[25]
Units: percentage of participants				
number (not applicable)	10.3	9.3	5.6	13.6

Notes:

[22] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[23] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[24] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

[25] - APaT; all randomized/enrolled receiving ≥1 dose of study treatment.

Statistical analyses

Statistical analysis title	Grazoprevir 100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 100 mg v Boceprevir 800 mg

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.1
upper limit	0.9

Statistical analysis title	Grazoprevir 200 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 200 mg v Boceprevir 800 mg
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-7.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.9
upper limit	2.5

Statistical analysis title	Grazoprevir 400 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 400 mg v Boceprevir 800 mg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	13.5

Statistical analysis title	Grazoprevir 800 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 800 mg v Boceprevir 800 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.1
upper limit	14.1

Statistical analysis title	Grazoprevir 400 mg/100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 400 mg/100 mg v Boceprevir 800 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.5
upper limit	9.6

Statistical analysis title	Grazoprevir 800 mg/100 mg vs. Boceprevir 800 mg

Statistical analysis description:

The percentage of participants that discontinued study medication due to an AE was evaluated for each grazoprevir arm in combination with Peg-IFN and RBV relative to the control boceprevir regimen. 95% confidence intervals for between-treatment differences in the percentage of participants with events were calculated using the Miettinen and Nurminen method.

Comparison groups	Grazoprevir 800 mg/100 mg v Boceprevir 800 mg

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	5.9

Secondary: Median Time to First Achievement of Undetectable HCV RNA During Treatment

End point title	Median Time to First Achievement of Undetectable HCV RNA During Treatment

End point description:

Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. Undetectable HCV RNA (target not detected [TND]) was defined as below the 9.3 IU/ml limit of detection. Kaplan Meier summary statistics were calculated for each treatment arm. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens. Participants in the FAS not achieving TND were censored.

End point type	Secondary

End point timeframe:

From first dose of study medication until first achievement of undetectable HCV RNA (up to 48 weeks of treatment)

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[26]	66[27]	68[28]	24[29]
Units: days				
median (confidence interval 95%)	22 (21 to 29)	15 (15 to 18)	28 (23 to 29)	16 (14 to 29)

Notes:

[26] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[27] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[28] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[29] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[30]	43[31]	36[32]	66[33]
Units: days				
median (confidence interval 95%)	16.5 (14 to 28)	27 (15 to 29)	29 (15 to 29)	57 (57 to 59)

Notes:

[30] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[31] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[32] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[33] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Rapid Viral Response (RVR)

End point title	Percentage of Participants Achieving Rapid Viral Response (RVR)

End point description:

Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. The Roche COBAS Taqman HCV Test, v2.0 assay (High Pure System) had a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL (in plasma). RVR was defined as undetectable (TND) HCV RNA at Week 4 of study therapy. 95% confidence intervals provided based on the Clopper-Pearson method. A Missing = Failure approach was used for missing data. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Secondary

End point timeframe:

After 4 weeks of treatment with grazoprevir/boceprevir

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[34]	66[35]	68[36]	24[37]
Units: percentage of participants				
number (confidence interval 95%)	72.2 (54.8 to 85.8)	90.9 (81.3 to 96.6)	91.2 (81.8 to 96.7)	87.5 (67.6 to 97.3)

Notes:

[34] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[35] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[36] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[37] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[38]	43[39]	36[40]	66[41]
Units: percentage of participants				
number (confidence interval 95%)	86.2 (68.3 to 96.1)	81.4 (66.6 to 91.6)	83.3 (67.2 to 93.6)	59.1 (46.3 to 71)

Notes:

[38] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[39] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[40] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[41] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Sustained Virologic Response 12 Weeks After the End of Study Therapy (SVR12)

End point title	Percentage of Participants Achieving Sustained Virologic Response 12 Weeks After the End of Study Therapy (SVR12)

End point description:

Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. The Roche COBAS Taqman HCV Test, v2.0 assay (High Pure System) had a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL (in plasma). SVR12 was defined as undetectable (TND) HCV RNA at 12 weeks after the end of all study therapy. 95% confidence intervals provided based on the Clopper-Pearson method. A Missing = Failure approach was used for missing data. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Secondary

End point timeframe:

12 weeks after the end of all treatment (up to 60 weeks)

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[42]	66[43]	68[44]	24[45]
Units: percentage of participants				
number (confidence interval 95%)	72.2 (54.8 to 85.8)	89.4 (79.4 to 95.6)	91.2 (81.8 to 96.7)	87.5 (67.6 to 97.3)

Notes:

[42] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[43] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[44] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[45] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[46]	43[47]	36[48]	66[49]
Units: percentage of participants				
number (confidence interval 95%)	79.3 (60.3 to 92)	93 (80.9 to 98.5)	91.7 (77.5 to 98.2)	60.6 (47.8 to 72.4)

Notes:

[46] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[47] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[48] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[49] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Sustained Virologic Response 24 Weeks After the End of Study Therapy (SVR24)

End point title	Percentage of Participants Achieving Sustained Virologic Response 24 Weeks After the End of Study Therapy (SVR24)

End point description:

Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. The Roche COBAS Taqman HCV Test, v2.0 assay (High Pure System) had a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL (in plasma). SVR24 was defined as undetectable (TND) HCV RNA at 24 weeks after the end of all study therapy. 95% confidence intervals provided based on the Clopper-Pearson method. A Missing = Failure approach was used for missing data. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Secondary

End point timeframe:

24 weeks after the end of all treatment (up to 72 weeks)

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[50]	66[51]	68[52]	24[53]
Units: percentage of participants				
number (confidence interval 95%)	72.2 (54.8 to 85.8)	86.4 (75.7 to 93.6)	92.6 (83.7 to 97.6)	87.5 (67.6 to 97.3)

Notes:

[50] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[51] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[52] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[53] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[54]	43[55]	36[56]	66[57]
Units: percentage of participants				
number (confidence interval 95%)	79.3 (60.3 to 92)	93 (80.9 to 98.5)	91.7 (77.5 to 98.2)	57.6 (44.8 to 69.7)

Notes:

[54] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[55] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[56] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[57] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Undetectable HCV RNA at Week 72

End point title	Percentage of Participants Achieving Undetectable HCV RNA at Week 72

End point description:

Blood was drawn from each participant to assess Hepatitis C Virus ribonucleic acid (HCV RNA) plasma levels using the Roche COBAS™ Taqman™ HCV Test, v2.0 at various time points prior to, during, and after dosing. Undetectable HCV RNA (target not detected [TND]) was defined as below the 9.3 IU/ml limit of detection. 95% confidence intervals provided based on the Clopper-Pearson method. A Missing = Failure approach was used for missing data. Results for participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

End point type	Secondary

End point timeframe:

Week 72

End point values	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg	Grazoprevir 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[58]	66[59]	68[60]	24[61]
Units: percentage of participants				
number (confidence interval 95%)	69.4 (51.9 to 83.7)	80.3 (68.7 to 89.1)	86.8 (76.4 to 93.8)	87.5 (67.6 to 97.3)

Notes:

[58] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[59] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[60] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[61] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

End point values	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[62]	43[63]	36[64]	66[65]
Units: percentage of participants				
number (confidence interval 95%)	75.9 (56.5 to 89.7)	79.1 (64 to 90)	83.3 (67.2 to 93.6)	54.5 (41.8 to 66.9)

Notes:

[62] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[63] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[64] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

[65] - FAS; all randomized/enrolled participants who received ≥1 dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study medication up to 72 weeks

Adverse event reporting additional description:

APaT population; all randomized/enrolled who received ≥1 dose of study treatment according to treatment actually received. Participants who received grazoprevir 400 or 800 mg and were then down-dosed to receive grazoprevir 100 mg are reported separately from participants who completed the 400 mg and 800 mg regimens.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	OL Grazoprevir 100 mg

Reporting group description:

TN cirrhotic participants received open-label Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 100 mg

Reporting group description:

TN NC participants received Grazoprevir 100 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 200 mg

Reporting group description:

TN NC participants received Grazoprevir 200 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 400 mg

Reporting group description:

TN NC participants received Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 800 mg

Reporting group description:

TN NC participants received Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 400 mg/100 mg

Reporting group description:

TN NC participants initially were randomized to receive Grazoprevir 400 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Grazoprevir 800 mg/100 mg

Reporting group description:

TN NC participants initially were randomized to receive Grazoprevir 800 mg + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy. As the result of an interim analysis, these participants were unblinded and transitioned to 100 mg grazoprevir once daily + Peg-IFN + RBV for 12 weeks followed by 12 or 36 weeks of Peg-IFN + RBV, based on response guided therapy.

Reporting group title	Boceprevir 800 mg

Reporting group description:

TN NC participants started a 4 week lead-in with Peg-IFN + RBV, then received Boceprevir 800 mg + Peg-IFN + RBV for 24 weeks followed by 0 or 20 weeks of Peg-IFN + RBV, based on response guided therapy.

Serious adverse events	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 36 (8.33%)	6 / 66 (9.09%)	9 / 68 (13.24%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent claudication			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizoaffective disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Segmented hyalinising vasculitis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Wound infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Grazoprevir 400 mg	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	2 / 29 (6.90%)	5 / 43 (11.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent claudication			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			

subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord polyp			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizoaffective disorder			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normochromic normocytic anaemia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Segmented hyalinising vasculitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast abscess			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 24 (8.33%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 36 (11.11%)	5 / 66 (7.58%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizoaffective disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			

subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Segmented hyalinising vasculitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	OL Grazoprevir 100 mg	Grazoprevir 100 mg	Grazoprevir 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 36 (94.44%)	64 / 66 (96.97%)	65 / 68 (95.59%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 36 (8.33%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	3	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 36 (22.22%)	14 / 66 (21.21%)	9 / 68 (13.24%)
occurrences (all)	9	19	9
Chest pain			
subjects affected / exposed	4 / 36 (11.11%)	2 / 66 (3.03%)	2 / 68 (2.94%)
occurrences (all)	4	2	3
Chills			
subjects affected / exposed	10 / 36 (27.78%)	20 / 66 (30.30%)	19 / 68 (27.94%)
occurrences (all)	11	22	20
Fatigue			
subjects affected / exposed	18 / 36 (50.00%)	27 / 66 (40.91%)	31 / 68 (45.59%)
occurrences (all)	19	30	38
Influenza like illness			
subjects affected / exposed	9 / 36 (25.00%)	14 / 66 (21.21%)	20 / 68 (29.41%)
occurrences (all)	9	15	22
Injection site erythema			
subjects affected / exposed	2 / 36 (5.56%)	12 / 66 (18.18%)	10 / 68 (14.71%)
occurrences (all)	2	12	10
Injection site irritation			
subjects affected / exposed	3 / 36 (8.33%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences (all)	3	1	0
Injection site rash			
subjects affected / exposed	1 / 36 (2.78%)	3 / 66 (4.55%)	6 / 68 (8.82%)
occurrences (all)	1	3	6
Injection site reaction			
subjects affected / exposed	2 / 36 (5.56%)	3 / 66 (4.55%)	5 / 68 (7.35%)
occurrences (all)	2	3	5
Oedema peripheral			

subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	3	0	0
Pain			
subjects affected / exposed	8 / 36 (22.22%)	12 / 66 (18.18%)	12 / 68 (17.65%)
occurrences (all)	8	13	12
Pyrexia			
subjects affected / exposed	9 / 36 (25.00%)	20 / 66 (30.30%)	24 / 68 (35.29%)
occurrences (all)	9	23	27
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 36 (19.44%)	5 / 66 (7.58%)	9 / 68 (13.24%)
occurrences (all)	7	5	9
Dyspnoea			
subjects affected / exposed	9 / 36 (25.00%)	6 / 66 (9.09%)	10 / 68 (14.71%)
occurrences (all)	10	8	12
Dyspnoea exertional			
subjects affected / exposed	0 / 36 (0.00%)	3 / 66 (4.55%)	6 / 68 (8.82%)
occurrences (all)	0	3	7
Epistaxis			
subjects affected / exposed	3 / 36 (8.33%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	3	0	1
Nasal congestion			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	1 / 68 (1.47%)
occurrences (all)	2	2	1
Oropharyngeal pain			
subjects affected / exposed	0 / 36 (0.00%)	4 / 66 (6.06%)	6 / 68 (8.82%)
occurrences (all)	0	4	7
Productive cough			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	0	1	1
Respiratory tract congestion			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	2 / 68 (2.94%)
occurrences (all)	2	0	2
Sinus congestion			

subjects affected / exposed	1 / 36 (2.78%)	3 / 66 (4.55%)	1 / 68 (1.47%)
occurrences (all)	1	3	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 36 (11.11%)	5 / 66 (7.58%)	10 / 68 (14.71%)
occurrences (all)	4	5	10
Apathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	4 / 36 (11.11%)	7 / 66 (10.61%)	11 / 68 (16.18%)
occurrences (all)	4	7	11
Insomnia			
subjects affected / exposed	8 / 36 (22.22%)	15 / 66 (22.73%)	10 / 68 (14.71%)
occurrences (all)	10	15	10
Irritability			
subjects affected / exposed	10 / 36 (27.78%)	16 / 66 (24.24%)	9 / 68 (13.24%)
occurrences (all)	10	16	11
Mood swings			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	2	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	3 / 68 (4.41%)
occurrences (all)	1	1	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	2 / 68 (2.94%)
occurrences (all)	0	0	2
Haemoglobin decreased			
subjects affected / exposed	3 / 36 (8.33%)	2 / 66 (3.03%)	4 / 68 (5.88%)
occurrences (all)	3	2	4
Spleen palpable			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	2 / 68 (2.94%)
occurrences (all)	1	1	2
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 36 (2.78%)	4 / 66 (6.06%)	8 / 68 (11.76%)
occurrences (all)	1	6	8
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 36 (0.00%)	4 / 66 (6.06%)	8 / 68 (11.76%)
occurrences (all)	0	4	9
Dizziness			
subjects affected / exposed	7 / 36 (19.44%)	6 / 66 (9.09%)	10 / 68 (14.71%)
occurrences (all)	8	6	10
Dysgeusia			
subjects affected / exposed	1 / 36 (2.78%)	5 / 66 (7.58%)	7 / 68 (10.29%)
occurrences (all)	1	5	7
Headache			
subjects affected / exposed	12 / 36 (33.33%)	28 / 66 (42.42%)	31 / 68 (45.59%)
occurrences (all)	16	39	35
Hypoaesthesia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 66 (1.52%)	6 / 68 (8.82%)
occurrences (all)	3	1	6
Migraine			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	1 / 68 (1.47%)
occurrences (all)	0	2	1
Paraesthesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Poor quality sleep			

subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 36 (36.11%)	11 / 66 (16.67%)	17 / 68 (25.00%)
occurrences (all)	16	16	21
Leukopenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	2 / 68 (2.94%)
occurrences (all)	0	3	3
Neutropenia			
subjects affected / exposed	7 / 36 (19.44%)	6 / 66 (9.09%)	7 / 68 (10.29%)
occurrences (all)	7	12	8
Thrombocytopenia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	4	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	2	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	1 / 68 (1.47%)
occurrences (all)	0	2	1
Eye irritation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	0 / 68 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	4 / 36 (11.11%)	3 / 66 (4.55%)	7 / 68 (10.29%)
occurrences (all)	5	3	8
Abdominal pain upper			

subjects affected / exposed	2 / 36 (5.56%)	7 / 66 (10.61%)	5 / 68 (7.35%)
occurrences (all)	2	7	6
Constipation			
subjects affected / exposed	3 / 36 (8.33%)	2 / 66 (3.03%)	3 / 68 (4.41%)
occurrences (all)	3	2	3
Diarrhoea			
subjects affected / exposed	5 / 36 (13.89%)	11 / 66 (16.67%)	11 / 68 (16.18%)
occurrences (all)	7	13	13
Dry mouth			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	5 / 68 (7.35%)
occurrences (all)	2	2	5
Dyspepsia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	7 / 68 (10.29%)
occurrences (all)	2	2	7
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	2	0	1
Nausea			
subjects affected / exposed	9 / 36 (25.00%)	25 / 66 (37.88%)	25 / 68 (36.76%)
occurrences (all)	10	29	28
Stomatitis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	2 / 68 (2.94%)
occurrences (all)	0	2	2
Toothache			
subjects affected / exposed	1 / 36 (2.78%)	4 / 66 (6.06%)	1 / 68 (1.47%)
occurrences (all)	1	5	1
Vomiting			
subjects affected / exposed	4 / 36 (11.11%)	8 / 66 (12.12%)	8 / 68 (11.76%)
occurrences (all)	4	13	10
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	2 / 68 (2.94%)
occurrences (all)	0	0	2
Jaundice			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	1	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 36 (22.22%)	17 / 66 (25.76%)	19 / 68 (27.94%)
occurrences (all)	8	17	20
Dry skin			
subjects affected / exposed	4 / 36 (11.11%)	6 / 66 (9.09%)	9 / 68 (13.24%)
occurrences (all)	4	6	10
Eczema			
subjects affected / exposed	1 / 36 (2.78%)	4 / 66 (6.06%)	0 / 68 (0.00%)
occurrences (all)	2	4	0
Erythema			
subjects affected / exposed	2 / 36 (5.56%)	4 / 66 (6.06%)	4 / 68 (5.88%)
occurrences (all)	2	4	5
Hyperhidrosis			
subjects affected / exposed	0 / 36 (0.00%)	7 / 66 (10.61%)	0 / 68 (0.00%)
occurrences (all)	0	9	0
Photosensitivity reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	6 / 36 (16.67%)	12 / 66 (18.18%)	15 / 68 (22.06%)
occurrences (all)	7	16	17
Pruritus generalised			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	3 / 68 (4.41%)
occurrences (all)	0	0	3
Rash			
subjects affected / exposed	8 / 36 (22.22%)	15 / 66 (22.73%)	13 / 68 (19.12%)
occurrences (all)	9	17	14
Rash erythematous			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	1	1	1
Scab			

subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	2	0	0
Xeroderma			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	1 / 68 (1.47%)
occurrences (all)	2	2	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	2 / 36 (5.56%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	2	1	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 36 (16.67%)	11 / 66 (16.67%)	9 / 68 (13.24%)
occurrences (all)	7	11	13
Back pain			
subjects affected / exposed	7 / 36 (19.44%)	5 / 66 (7.58%)	4 / 68 (5.88%)
occurrences (all)	7	5	4
Muscle spasms			
subjects affected / exposed	4 / 36 (11.11%)	1 / 66 (1.52%)	1 / 68 (1.47%)
occurrences (all)	4	1	1
Myalgia			
subjects affected / exposed	6 / 36 (16.67%)	12 / 66 (18.18%)	9 / 68 (13.24%)
occurrences (all)	6	13	11
Neck pain			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	1 / 68 (1.47%)
occurrences (all)	1	2	1
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	4 / 68 (5.88%)
occurrences (all)	0	0	5
Infections and infestations			

Bronchitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	3 / 68 (4.41%)
occurrences (all)	2	0	3
Ear infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	0 / 68 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	4 / 68 (5.88%)
occurrences (all)	0	2	4
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	2 / 68 (2.94%)
occurrences (all)	0	1	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	3 / 66 (4.55%)	6 / 68 (8.82%)
occurrences (all)	0	3	6
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 36 (11.11%)	16 / 66 (24.24%)	11 / 68 (16.18%)
occurrences (all)	4	17	11
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Grazoprevir 400 mg	Grazoprevir 800 mg	Grazoprevir 400 mg/100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 24 (95.83%)	27 / 29 (93.10%)	42 / 43 (97.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	4 / 43 (9.30%)
occurrences (all)	1	1	4
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	5 / 24 (20.83%)	3 / 29 (10.34%)	7 / 43 (16.28%)
occurrences (all)	5	4	8
Chest pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Chills			
subjects affected / exposed	6 / 24 (25.00%)	10 / 29 (34.48%)	12 / 43 (27.91%)
occurrences (all)	7	10	12
Fatigue			
subjects affected / exposed	11 / 24 (45.83%)	16 / 29 (55.17%)	17 / 43 (39.53%)
occurrences (all)	12	19	17
Influenza like illness			
subjects affected / exposed	7 / 24 (29.17%)	5 / 29 (17.24%)	15 / 43 (34.88%)
occurrences (all)	7	5	15
Injection site erythema			
subjects affected / exposed	1 / 24 (4.17%)	8 / 29 (27.59%)	2 / 43 (4.65%)
occurrences (all)	1	8	2
Injection site irritation			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Injection site rash			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	2 / 43 (4.65%)
occurrences (all)	1	0	2
Oedema peripheral			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	3 / 24 (12.50%)	11 / 29 (37.93%)	8 / 43 (18.60%)
occurrences (all)	3	11	8
Pyrexia			

subjects affected / exposed	12 / 24 (50.00%)	8 / 29 (27.59%)	12 / 43 (27.91%)
occurrences (all)	12	10	18
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 24 (4.17%)	4 / 29 (13.79%)	9 / 43 (20.93%)
occurrences (all)	1	5	10
Dyspnoea			
subjects affected / exposed	1 / 24 (4.17%)	3 / 29 (10.34%)	2 / 43 (4.65%)
occurrences (all)	1	5	2
Dyspnoea exertional			
subjects affected / exposed	0 / 24 (0.00%)	6 / 29 (20.69%)	6 / 43 (13.95%)
occurrences (all)	0	6	6
Epistaxis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	2 / 43 (4.65%)
occurrences (all)	0	1	2
Nasal congestion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 24 (8.33%)	4 / 29 (13.79%)	1 / 43 (2.33%)
occurrences (all)	2	4	1
Productive cough			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Respiratory tract congestion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Sinus congestion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	3 / 43 (6.98%)
occurrences (all)	0	0	3
Apathy			

subjects affected / exposed	0 / 24 (0.00%)	3 / 29 (10.34%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
Depression			
subjects affected / exposed	1 / 24 (4.17%)	5 / 29 (17.24%)	6 / 43 (13.95%)
occurrences (all)	1	5	6
Insomnia			
subjects affected / exposed	3 / 24 (12.50%)	6 / 29 (20.69%)	7 / 43 (16.28%)
occurrences (all)	3	7	7
Irritability			
subjects affected / exposed	1 / 24 (4.17%)	3 / 29 (10.34%)	7 / 43 (16.28%)
occurrences (all)	1	3	7
Mood swings			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 24 (4.17%)	4 / 29 (13.79%)	4 / 43 (9.30%)
occurrences (all)	1	4	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	3 / 29 (10.34%)	2 / 43 (4.65%)
occurrences (all)	0	3	2
Blood bilirubin increased			
subjects affected / exposed	2 / 24 (8.33%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	2	1	0
Haemoglobin decreased			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Spleen palpable			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	1 / 24 (4.17%)	3 / 29 (10.34%)	0 / 43 (0.00%)
occurrences (all)	1	3	0
Injury, poisoning and procedural complications			

Accidental overdose			
subjects affected / exposed	3 / 24 (12.50%)	6 / 29 (20.69%)	3 / 43 (6.98%)
occurrences (all)	3	6	5
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	4 / 43 (9.30%)
occurrences (all)	0	0	4
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	2 / 43 (4.65%)
occurrences (all)	1	0	3
Dizziness			
subjects affected / exposed	2 / 24 (8.33%)	6 / 29 (20.69%)	5 / 43 (11.63%)
occurrences (all)	2	6	6
Dysgeusia			
subjects affected / exposed	3 / 24 (12.50%)	3 / 29 (10.34%)	1 / 43 (2.33%)
occurrences (all)	3	3	1
Headache			
subjects affected / exposed	8 / 24 (33.33%)	12 / 29 (41.38%)	12 / 43 (27.91%)
occurrences (all)	8	16	13
Hypoaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Poor quality sleep			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 24 (8.33%)	7 / 29 (24.14%)	5 / 43 (11.63%)
occurrences (all)	2	7	7
Leukopenia			

subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
Neutropenia			
subjects affected / exposed	2 / 24 (8.33%)	1 / 29 (3.45%)	2 / 43 (4.65%)
occurrences (all)	3	2	3
Thrombocytopenia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 24 (8.33%)	1 / 29 (3.45%)	1 / 43 (2.33%)
occurrences (all)	2	1	1
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 24 (8.33%)	2 / 29 (6.90%)	3 / 43 (6.98%)
occurrences (all)	2	2	3
Eye irritation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	3 / 43 (6.98%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Abdominal pain upper			
subjects affected / exposed	2 / 24 (8.33%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	2	2	0
Constipation			
subjects affected / exposed	2 / 24 (8.33%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Diarrhoea			

subjects affected / exposed	5 / 24 (20.83%)	11 / 29 (37.93%)	5 / 43 (11.63%)
occurrences (all)	6	14	5
Dry mouth			
subjects affected / exposed	2 / 24 (8.33%)	1 / 29 (3.45%)	2 / 43 (4.65%)
occurrences (all)	2	1	2
Dyspepsia			
subjects affected / exposed	3 / 24 (12.50%)	2 / 29 (6.90%)	2 / 43 (4.65%)
occurrences (all)	3	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
Nausea			
subjects affected / exposed	6 / 24 (25.00%)	16 / 29 (55.17%)	15 / 43 (34.88%)
occurrences (all)	8	21	17
Stomatitis			
subjects affected / exposed	2 / 24 (8.33%)	1 / 29 (3.45%)	1 / 43 (2.33%)
occurrences (all)	2	1	1
Toothache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	6 / 24 (25.00%)	5 / 29 (17.24%)	4 / 43 (9.30%)
occurrences (all)	8	7	9
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Jaundice			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 24 (29.17%)	9 / 29 (31.03%)	8 / 43 (18.60%)
occurrences (all)	7	10	8
Dry skin			

subjects affected / exposed	1 / 24 (4.17%)	2 / 29 (6.90%)	7 / 43 (16.28%)
occurrences (all)	1	2	7
Eczema			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Erythema			
subjects affected / exposed	1 / 24 (4.17%)	2 / 29 (6.90%)	3 / 43 (6.98%)
occurrences (all)	1	2	3
Hyperhidrosis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	2 / 43 (4.65%)
occurrences (all)	0	2	2
Photosensitivity reaction			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	6 / 24 (25.00%)	7 / 29 (24.14%)	4 / 43 (9.30%)
occurrences (all)	6	7	4
Pruritus generalised			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Rash			
subjects affected / exposed	3 / 24 (12.50%)	6 / 29 (20.69%)	7 / 43 (16.28%)
occurrences (all)	7	7	12
Rash erythematous			
subjects affected / exposed	2 / 24 (8.33%)	2 / 29 (6.90%)	2 / 43 (4.65%)
occurrences (all)	3	4	7
Rash pruritic			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Scab			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Skin exfoliation			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Xeroderma			

subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 24 (29.17%)	4 / 29 (13.79%)	3 / 43 (6.98%)
occurrences (all)	8	7	3
Back pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	2 / 43 (4.65%)
occurrences (all)	0	3	2
Muscle spasms			
subjects affected / exposed	1 / 24 (4.17%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	6 / 24 (25.00%)	4 / 29 (13.79%)	7 / 43 (16.28%)
occurrences (all)	9	5	7
Neck pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Pain in extremity			
subjects affected / exposed	2 / 24 (8.33%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Ear infection			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0

Influenza			
subjects affected / exposed	2 / 24 (8.33%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 29 (6.90%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	3 / 43 (6.98%)
occurrences (all)	0	1	4
Upper respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 29 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 24 (16.67%)	9 / 29 (31.03%)	10 / 43 (23.26%)
occurrences (all)	5	9	10
Dehydration			
subjects affected / exposed	0 / 24 (0.00%)	1 / 29 (3.45%)	0 / 43 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Grazoprevir 800 mg/100 mg	Boceprevir 800 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 36 (100.00%)	64 / 66 (96.97%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 36 (22.22%)	12 / 66 (18.18%)	
occurrences (all)	8	13	
Chest pain			

subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	
occurrences (all)	2	2	
Chills			
subjects affected / exposed	11 / 36 (30.56%)	15 / 66 (22.73%)	
occurrences (all)	12	16	
Fatigue			
subjects affected / exposed	15 / 36 (41.67%)	27 / 66 (40.91%)	
occurrences (all)	16	30	
Influenza like illness			
subjects affected / exposed	7 / 36 (19.44%)	23 / 66 (34.85%)	
occurrences (all)	7	24	
Injection site erythema			
subjects affected / exposed	3 / 36 (8.33%)	8 / 66 (12.12%)	
occurrences (all)	3	9	
Injection site irritation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Injection site rash			
subjects affected / exposed	0 / 36 (0.00%)	4 / 66 (6.06%)	
occurrences (all)	0	4	
Injection site reaction			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	4 / 36 (11.11%)	12 / 66 (18.18%)	
occurrences (all)	4	13	
Pyrexia			
subjects affected / exposed	6 / 36 (16.67%)	20 / 66 (30.30%)	
occurrences (all)	22	21	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	6 / 36 (16.67%)	7 / 66 (10.61%)	
occurrences (all)	6	8	
Dyspnoea			
subjects affected / exposed	4 / 36 (11.11%)	7 / 66 (10.61%)	
occurrences (all)	4	7	
Dyspnoea exertional			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	
occurrences (all)	0	2	
Nasal congestion			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	3 / 36 (8.33%)	6 / 66 (9.09%)	
occurrences (all)	3	7	
Productive cough			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Respiratory tract congestion			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Sinus congestion			
subjects affected / exposed	2 / 36 (5.56%)	3 / 66 (4.55%)	
occurrences (all)	3	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 36 (8.33%)	3 / 66 (4.55%)	
occurrences (all)	3	3	
Apathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	8 / 36 (22.22%)	7 / 66 (10.61%)	
occurrences (all)	8	7	

Insomnia			
subjects affected / exposed	8 / 36 (22.22%)	21 / 66 (31.82%)	
occurrences (all)	10	22	
Irritability			
subjects affected / exposed	5 / 36 (13.89%)	12 / 66 (18.18%)	
occurrences (all)	7	14	
Mood swings			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Haemoglobin decreased			
subjects affected / exposed	1 / 36 (2.78%)	5 / 66 (7.58%)	
occurrences (all)	1	8	
Spleen palpable			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	5 / 36 (13.89%)	3 / 66 (4.55%)	
occurrences (all)	5	3	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	
occurrences (all)	0	2	

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	2	1	
Dizziness			
subjects affected / exposed	5 / 36 (13.89%)	9 / 66 (13.64%)	
occurrences (all)	6	9	
Dysgeusia			
subjects affected / exposed	4 / 36 (11.11%)	19 / 66 (28.79%)	
occurrences (all)	4	19	
Headache			
subjects affected / exposed	17 / 36 (47.22%)	35 / 66 (53.03%)	
occurrences (all)	19	44	
Hypoaesthesia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	2	4	
Migraine			
subjects affected / exposed	0 / 36 (0.00%)	3 / 66 (4.55%)	
occurrences (all)	0	4	
Paraesthesia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 66 (1.52%)	
occurrences (all)	2	1	
Poor quality sleep			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 36 (19.44%)	18 / 66 (27.27%)	
occurrences (all)	7	25	
Leukopenia			
subjects affected / exposed	0 / 36 (0.00%)	5 / 66 (7.58%)	
occurrences (all)	0	9	
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)	11 / 66 (16.67%)	
occurrences (all)	0	13	
Thrombocytopenia			

subjects affected / exposed	0 / 36 (0.00%)	3 / 66 (4.55%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	
occurrences (all)	2	2	
Eye irritation			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	
occurrences (all)	2	0	
Visual acuity reduced			
subjects affected / exposed	2 / 36 (5.56%)	1 / 66 (1.52%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)	4 / 66 (6.06%)	
occurrences (all)	1	4	
Abdominal pain upper			
subjects affected / exposed	5 / 36 (13.89%)	4 / 66 (6.06%)	
occurrences (all)	5	4	
Constipation			
subjects affected / exposed	3 / 36 (8.33%)	4 / 66 (6.06%)	
occurrences (all)	4	4	
Diarrhoea			
subjects affected / exposed	12 / 36 (33.33%)	16 / 66 (24.24%)	
occurrences (all)	13	19	
Dry mouth			
subjects affected / exposed	2 / 36 (5.56%)	1 / 66 (1.52%)	
occurrences (all)	2	1	
Dyspepsia			

subjects affected / exposed	4 / 36 (11.11%)	3 / 66 (4.55%)	
occurrences (all)	4	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)	5 / 66 (7.58%)	
occurrences (all)	0	5	
Nausea			
subjects affected / exposed	19 / 36 (52.78%)	31 / 66 (46.97%)	
occurrences (all)	29	37	
Stomatitis			
subjects affected / exposed	0 / 36 (0.00%)	6 / 66 (9.09%)	
occurrences (all)	0	6	
Toothache			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	6 / 36 (16.67%)	16 / 66 (24.24%)	
occurrences (all)	7	20	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 66 (0.00%)	
occurrences (all)	2	0	
Jaundice			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 36 (27.78%)	8 / 66 (12.12%)	
occurrences (all)	10	8	
Dry skin			
subjects affected / exposed	5 / 36 (13.89%)	8 / 66 (12.12%)	
occurrences (all)	5	8	
Eczema			
subjects affected / exposed	2 / 36 (5.56%)	1 / 66 (1.52%)	
occurrences (all)	2	1	
Erythema			

subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	
occurrences (all)	0	2	
Hyperhidrosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	10 / 36 (27.78%)	10 / 66 (15.15%)	
occurrences (all)	11	12	
Pruritus generalised			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	9 / 36 (25.00%)	17 / 66 (25.76%)	
occurrences (all)	10	22	
Rash erythematous			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	3	3	
Rash pruritic			
subjects affected / exposed	0 / 36 (0.00%)	4 / 66 (6.06%)	
occurrences (all)	0	4	
Scab			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Skin exfoliation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Xeroderma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 66 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 66 (0.00%)	
occurrences (all)	1	0	

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 36 (2.78%)	5 / 66 (7.58%)	
occurrences (all)	1	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 36 (19.44%)	12 / 66 (18.18%)	
occurrences (all)	7	15	
Back pain			
subjects affected / exposed	5 / 36 (13.89%)	3 / 66 (4.55%)	
occurrences (all)	7	3	
Muscle spasms			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Myalgia			
subjects affected / exposed	5 / 36 (13.89%)	13 / 66 (19.70%)	
occurrences (all)	6	15	
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)	2 / 66 (3.03%)	
occurrences (all)	0	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 36 (5.56%)	2 / 66 (3.03%)	
occurrences (all)	2	3	
Ear infection			
subjects affected / exposed	1 / 36 (2.78%)	2 / 66 (3.03%)	
occurrences (all)	1	2	
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 66 (1.52%)	
occurrences (all)	0	1	

Pneumonia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	5 / 66 (7.58%)	
occurrences (all)	0	5	
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 66 (1.52%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 36 (38.89%)	15 / 66 (22.73%)	
occurrences (all)	14	16	
Dehydration			
subjects affected / exposed	3 / 36 (8.33%)	0 / 66 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2011	Protocol amendment 1 (AM1) added the response-guided therapy regimen for the boceprevir control arm, revised the criteria for virologic failure for all arms, included changes to the prohibited concomitant medications, and removed Area under the concentration-time curve as a pharmacokinetic (PK) endpoint.
29 September 2011	AM2 added a semen analysis substudy to the study flow chart, added exclusion criteria for the semen analysis substudy, changed the missing data approach, and updated guidance for missed doses of grazoprevir.
26 January 2012	AM3 revised protocol text, study diagram, flow chart, study objectives, eligibility criteria, and statistical analysis text to include a prior treatment failure and compensated cirrhotic patient cohort. AM3 also added a second planned interim analysis and modified AE and blood chemistry analysis.
10 April 2012	AM4 revised text throughout the protocol to remove the prior treatment failure and compensated cirrhotic patient cohort and added text throughout the protocol describing results and actions related to the first interim analysis including the down-dosing of patients in the 400 mg and 800 mg grazoprevir arms to 100 mg
04 January 2013	AM5 added a cohort to study 100 mg grazoprevir in combination with PEG-IFN and RBV in treatment-naïve cirrhotic patients and revised eligibility criteria for this new cohort accordingly.
29 March 2013	AM6 added a dosing duration modification for the cirrhotic cohort assigned to the 24-week treatment duration, and made revisions to the study flow chart, eligibility criteria, PK Analysis section, and HCV RNA analysis section in relation to the cirrhotic cohort.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported